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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,966	11/17/1999	RODERICK L. HALL	98.736-A	5234

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 02/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,966	HALL ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,15-21 and 23-25* is/are pending in the application.

4a) Of the above claim(s) *18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,15-17,19 and 23-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix A*.

DETAILED ACTION

Status of the Application

[1] Claims 1-10, 15-21, and 23-25 are pending in the application.

[2] Applicant's amendment to the claims, filed 11/14/2005, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's arguments filed on 11/14/2005 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[5] Claims 18 and 20-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

[6] Claims 1-10, 15-17, 19, and 23-25 are being examined on the merits only to the extent the claims read on the elected subject matter. In view of applicant's amendment to claim 15 to remove improper multiple dependency, the objection to claims 16-17 is withdrawn and claims 16-17 have been herein treated on the merits.

Claim Objection(s)

[7] Claims 15 and 19 remain objected to in the use of an improper sequence identifier. It is suggested that applicants use the proper sequence identifier "SEQ ID NO:" in the claims. See 37 CFR 1.821(d). Appropriate correction is required.

[8] Claim 15 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112, First Paragraph

[9] Claims 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. This is a new matter rejection.

Claims 23-25 limit the activity of the inhibitor to inhibiting sodium channels, optionally wherein the sodium channel is an epithelial sodium channel or to increasing TMV in the subject. MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description". Applicant points to Examples 17-26 at pp. 71-85 of the specification

as showing support for the recited limitations of claims 23-25. However, the recited claim limitations go beyond the subject matter originally filed.

Examples 17-26 teach purification of placental Bikunin (1-170) from cultured CHO cells and measuring various effects of placental Bikunin (1-170) on cultured mammalian cells, sheep, and guinea pigs. The species of cultured mammalian cells, sheep, and guinea pigs fails to support the genus of subjects as recited in claim 1. Even assuming *arguendo* the species supported the broader genus, the examiner can find no teaching wherein SEQ ID NO:8 inhibits sodium channels, inhibits epithelial sodium channels, and/or increases TMV.

It is suggested that applicants "show support" for the claim in accordance with 35 U.S.C. 112, first paragraph, and MPEP § 2163.

Claim Rejections - 35 USC § 103

[10] The rejection of claims 1-10, 15, and 19 under 35 U.S.C. 103(a) as being unpatentable over Tamburini et al. in view of Rasche et al. and O'Riordan et al. is maintained for the reasons of record and the reasons stated below. Claims 16-17 and new claims 23-25 are included in the instant rejection. Thus, claims 1-10, 15-17, 19, and 23-25 are rejected.

RESPONSE TO ARGUMENT: Applicant argues there is no motivation to combine the cited references. Addressing the references individually, applicant argues Tamburini et al. does not teach a method of accelerating the rate of mucocilliary clearance, Rasche et al. does not teach a Kunitz-type inhibitor to accelerate the rate of

mucocilliary clearance, and O'Riordan et al. does not teach a Kunitz-type inhibitor can be used to treat mucocilliary impairment.

Applicant's argument is not found persuasive. As acknowledged by applicant, one cannot show non-obviousness by attacking each reference individually where the rejection is based on the combination. As in the previous response, applicant argues against each reference individually, without acknowledging the combined teachings. As noted in the prior Office action, there is motivation to combine the cited references as Tamburini et al. teaches SEQ ID NO:8 can be used as a neutrophil elastase inhibitor in place of aprotinin for treatment of pulmonary emphysema, Rasche et al. teaches aprotinin administration in patients suffering from chronic obstructive bronchitis including patients suffering from emphasematous pulmonary changes had improved expectoration by the patient and a liquification of the sputum, and O'Riordan et al. teaches inhibition of neutrophil elastase results in increased mucociliary clearance and suggests that elastase inhibitors may be useful in the treatment of mucociliary dysfunction in asthma. While no single reference teaches administering SEQ ID NO:8 to increase the rate of mucocilliary clearance, it is the combination of references that teaches the invention and provides motivation and a reasonable expectation of success.

Applicant argues there is no reasonable expectation of success because, in view of the teachings of Laube et al., one of ordinary skill in the art would recognize that affecting elastase activity or levels does not correlate or is not relevant to accelerating the rate of mucocilliary clearance.

Applicant's argument is not found persuasive. According to applicant, DNAse 1 is "a protease inhibitor." The art recognizes DNAse I as a deoxyribonuclease, not as a protease inhibitor as asserted by applicant (see Appendix A). According to Laube et al., DNA released by inflammatory cells further increases the viscosity of cystic fibrosis viscosity (p. 752, left column, middle). Laube et al. sought to determine the effect of DNAse 1 degradation of the inflammatory cell-released DNA on airflow obstruction and mucocilliary clearance. There is no indication in the reference of Laube et al. that administration of DNAse 1 was to affect the activity or level of elastase. Thus, one of ordinary skill in the art at the time of the invention would recognize that the reference of Laube et al. is not relevant to the determination of whether the combination of references provides a reasonable expectation of success.

According to applicant, not all claim limitations are taught by the combination of references. Applicant argues that as a whole, the claimed invention describes that Kunitz-type inhibitors accelerate the rate of mucocilliary clearance by inhibiting sodium channels and affecting the potential difference, thereby increasing the TMV. Applicant argues that as a whole the invention does not imply or indicate inhibiting proteases by increasing levels of protease inhibitors. Applicant argues that the problem to be solved by the claimed invention is that Kunitz-type inhibitors inhibit sodium channels and reduce potential difference, thereby decreasing TMV. Applicant cites the references of Bridges et al. and Donaldson et al. as describing and further supporting the disclosure of the claimed invention. According to applicant, in view of these references, "the claimed invention was the first to disclose and suggest a direct role of a protease not yet

reported and which inhibition may affect Na+ transport as a method to accelerate of mucociliary clearance."

Applicant's argument is not found persuasive. In this case, there is no requirement that the combined references teach that Kunitz-type inhibitors accelerate the rate of mucocilliary clearance by inhibiting sodium channels and affecting the potential difference, thereby increasing the TMV. MPEP 2144 makes clear that "[i]t is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant." Here, the claimed invention only requires administering an effective mucociliary clearance stimulatory amount of a composition comprising SEQ ID NO:8, thereby accelerating mucociliary clearance, which is taught by the combination of references. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the claimed invention describes that Kunitz-type inhibitors accelerate the rate of mucocilliary clearance by inhibiting sodium channels and affecting the potential difference, thereby increasing the TMV) are not recited in rejected claim(s) 1-10, 15-17, and 19. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, although claims 23-25 limit the activity of the inhibitor to inhibiting sodium channels, optionally wherein the sodium channel is an epithelial sodium channel or to increasing TMV in the subject, absent evidence to the contrary, these are inherent features of the peptide of Tamburini et al. There is no requirement that a person of ordinary skill in the

art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. See MPEP 2112. The peptide of SEQ ID NO:8 is taught by Tamburini et al. and the administration of this peptide for accelerating mucocilliary clearance in a subject is taught by the combination of references.

Conclusion

[11] Status of the claims:

Claims 1-10, 15-21, and 23-25 are pending.

Claims 18 and 20-21 are withdrawn from consideration.

Claims 1-10, 15-17, 19, and 23-25 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Thursday, 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656

IUBMB Enzyme Nomenclature

EC 3.1.21.1

Common name: deoxyribonuclease I

Reaction: Endonucleolytic cleavage to 5'-phosphodinucleotide and 5'-phosphooligonucleotide end-products

Other name(s): pancreatic DNase; DNase; thymonuclease, dornase; dornava; dornavac; pancreatic deoxyribonuclease; pancreatic dornase; deoxyribonuclease (pancreatic); pancreatic DNase; DNAase; deoxyribonucleic phosphatase; DNase I; alkaline deoxyribonuclease; alkaline DNase; endodeoxyribonuclease I; DNA depolymerase; *Escherichia coli* endonuclease I; deoxyribonuclease A; DNA endonuclease; DNA nuclease

Comments: Preference for double-stranded DNA. Formerly EC 3.1.4.5.

Links to other databases: BRENDA, EXPASY, KEGG, ERGO, PDB, CAS registry number: 9003-98-9

References:

1. Privat de Garilhe, M. and Laskowski, M. Study of the enzymatic degradation of deoxyribonucleic acid by two different deoxyribonucleodepolymerases. *J. Biol. Chem.* 215 (1955) 269-276.

2. Kunitz, M. Isolation of crystalline deoxyribonuclease from beef pancreas. *Science* 108 (1948) 19-20.

3. Laskowski, M., Sr. Venom exonuclease, in Boyer, P.D. (Ed.), *The Enzymes*, 3rd edn., vol. 4, Academic Press, New York, 1971, pp. 313-328.

[EC 3.1.21.1 created 1961 as EC 3.1.4.5, transferred 1978 to EC 3.1.21.1, modified 1981]

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